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Marchiafava-Bignami disease: a rare entity with a poor outcome

Doença de Marchiafava-Bignami: uma rara entidade com prognóstico sombrio

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ABSTRACT

Marchiafava-Bignami disease is a rare affliction characterized by primary degeneration of the corpus callosum associated with chronic consumption of ethanol. The disease may occasionally occur in patients who are not alcoholics but are chronically malnourished. A complex deficiency of group B vitamins is the main etiopathogenic hypothesis, and many patients improve after the administration of these compounds. However, a good response is not always observed. The definitive diagnosis of Marchiafava-Bignami disease can be problematic and is based on features of neuroimaging studies, especially magnetic resonance imaging. Its treatment is still controversial and shows variable results. Because nutritional factors are implicated, as in Wernicke's encephalopathy, some

authors claim that replacement of B vitamins is beneficial. The present article is a case report of a severe acute form of Marchiafava-Bignami disease in an alcohol-dependent male patient who improved after the administration of parenteral B vitamins. As a consequence of his neurological and immunologic conditions, he developed multiple pulmonary infections and had a protracted course in the intensive care unit. He eventually died of sepsis associated with an uncommon fungus, *Rhodotorula mucilaginosa*. The present article reports the clinical and neuroimaging data from this patient and contains a review of Marchiafava-Bignami disease and *Rhodotorula* infections in the intensive care unit.

Keywords: Brain diseases; Marchiafava-Bignami disease/diagnosis; Alcoholism/complications; Infection; Magnetic resonance imaging; Case reports

INTRODUCTION

Marchiafava-Bignami disease (MBD) is characterized by primary degeneration of the corpus callosum associated with chronic alcohol consumption.⁽¹⁾ However, it can occur in patients who do not use alcohol.^(2,3) The main hypothesis for its pathogenesis is that the disease is a result of B vitamin deficiency. Although many patients may improve after administration of B vitamins, others do not. In these cases, morbidity and mortality are relatively high:⁽⁴⁾ as of 2004, approximately 250 patients had been described, 200 had died, 30 suffered from severe dementia, and only 20 experienced positive outcomes. It seems that with alcoholism, the prognosis is worse.

The original description of the disease was in made in 1903 in central Italy and was thought to be related to the consumption of large amounts of low-cost Chianti.⁽¹⁾ It is now known that MBD is widely observed and can be caused by any alcoholic beverage. The vast majority of patients are male, are between 40 and 60 years of age, and have a history of chronic alcoholism and malnutrition.⁽¹⁻⁶⁾ The diagnosis is difficult and generally is a result of neuroimaging, particularly magnetic resonance imaging (MRI).⁽⁵⁻⁸⁾ The treatment of MBD is still controversial and shows variable results. The implication of nutritional factors, similar to Wernicke's encephalopathy, suggests that replacement of B vitamins is beneficial. However, with the variable response to this type of therapy, corticosteroids and amantadine have been proposed by some authors.⁽⁹⁻¹¹⁾

CASE REPORT

This is a case report of a 51-year-old white male patient who had a history of severe alcoholism with a high daily consumption of alcohol over 30 years. His family reported that he consumed rum, cognac and wines. He refused to treat his addiction. One year prior to presentation, his family observed a decrease in his short-term memory, and he complained of paresthesias of the lower and upper limbs. After an ingestion of large amounts of alcohol, excessive drowsiness quickly evolved into torpor and then a coma. He was taken to the Hospital Universitário of Universidade Estadual do Oeste do Paraná (Unioeste). On admission, his Glasgow coma score was 7, and he showed no signs of meningeal irritation, focal deficits or cranial nerve abnormalities. IV thiamine (500 mg/

day) and high doses of parenteral B vitamins were administered.

Cranial computerized tomography scan (CT) revealed a hypodensity in the corpus callosum, which was better characterized by MRI. MRI showed involvement of the cortical regions and subcortical white matter of both frontal lobes as well as small areas of the post-central and superior temporal gyri with no signs of disruption of the blood-brain barrier (Figures 1, 2 and 3). A mild improvement in his level of consciousness was observed (Glasgow = 10) with mechanical ventilatory support, but the patient developed multiple pulmonary infectious complications and remained in the intensive care unit (ICU) with respiratory insufficiency dependent on mechanical ventilation. He received a tracheostomy. After more than 10 weeks in the ICU, he became septic, exhibiting a fever along with worsening of his respiratory status. Over the course of 24 hours, his hemodynamic condition deteriorated, and both vasoactive drugs and broad-spectrum IV antibiotics were started without success. Cultures of blood and tracheal secretions revealed an uncommon fungus (*Rhodotorula mucilaginosa*). Amphotericin B treatment was begun, but there was no significant response, and he eventually succumbed to septic shock.

DISCUSSION

There is no prototypical clinical presentation of MBD. Subtle clinical signs such as reduced consciousness, emotional and psychotic symptoms, depression and apathy, aggression, seizures, hemiparesis, ataxia, and apraxia may be present as initial manifestations.⁽⁵⁾ However, their development can lead to coma and death. The disease can be acute, subacute, or chronic and may lead to death within weeks or months. The acute form of MBD includes seizures, decreased consciousness and rapid death. The subacute form includes varying degrees of confusion, dysarthria, behavioral abnormalities, memory deficits, signs of interhemispheric disconnection, apraxia, and gait disorders.⁽¹²⁾ It is worth noting that both acute and subacute MBD can produce an extensive list of neurological manifestations that are frequently observed in the ICU. However, MBD is rarely proposed as a potential cause of these symptoms. The chronic form, which is less common, is characterized by mild dementia, but it can be progressive and is not frequently observed in the ICU.

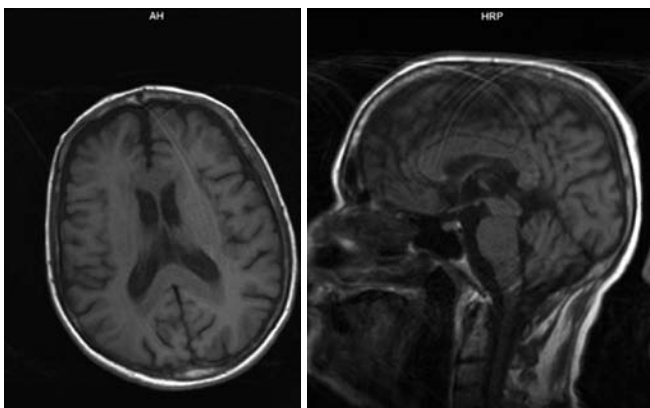


Figure 1 – T1-weighted MRI images showing hypointense lesions in the corpus callosum.

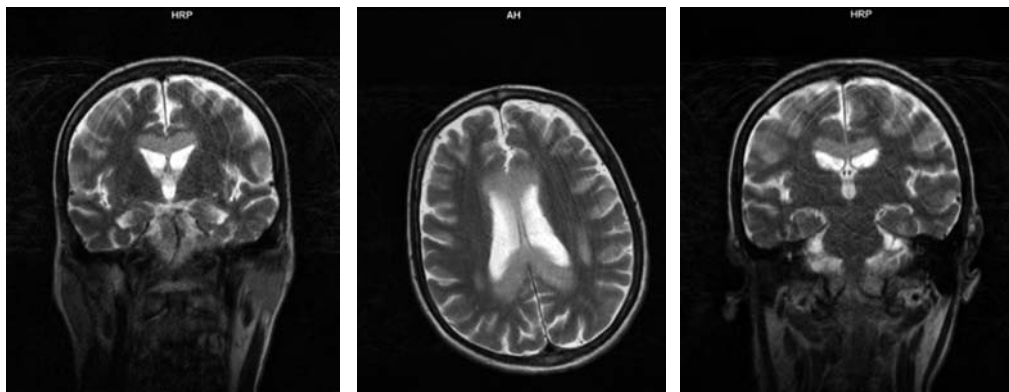


Figure 2 – T2-weighted MRI images showing hyperintense lesions in the corpus callosum.

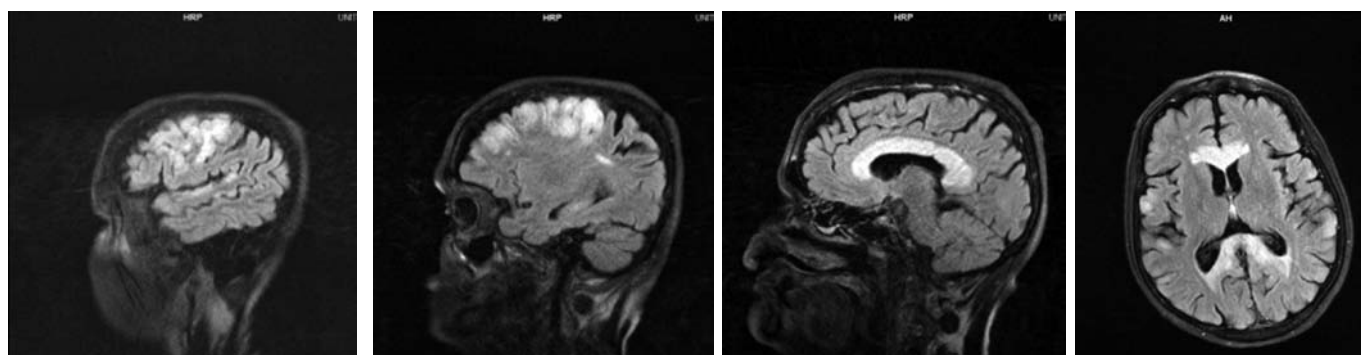


Figure 3 – T2-FLAIR (fluid attenuation inversion recovery) - weighted MRI images showing hyperintense lesions in the corpus callosum and frontal lobe (subcortical and cortical).

Until recently, a definitive diagnosis of MBD could only be made at autopsy. However, in the era of modern neuroimaging, it is possible to confirm the diagnosis based on a typical clinical profile with a past history of alcoholism and a CT scan or MRI demonstrating specific pathological lesions in the corpus callosum.⁽⁵⁻⁷⁾ The corpus callosum appears hypodense on CT scans, except for cases characterized by subacute hemorrhage, in which the lesions may be isodense or hyperdense. However, when the lesion is small, the CT tends to be normal. In these cases, MRI has greater sensitivity. Callosal injuries are typically hypointense on T1 and hyperintense on T2, sometimes extending to the genu and adjacent white matter. The lesions do not present with a mass effect and, in the acute phase, may present with contrast enhancement. Chronic lesions may progress to “cavitation” with well-defined margins. This is called a “positive sandwich sign”. The hyperintensities can be found in other regions, such as the semiovalle centrum.⁽⁵⁻⁷⁾

As the etiology of this disease remains uncertain, specific and well-defined therapy is not available. Treatment with thiamine and other B vitamins, including vitamin B-12 and folic acid, has been used in many patients who have

recovered. However, therapeutic failure is not uncommon, even if treatment is started at the beginning of symptoms.⁽¹²⁾ Seizures and coma are treated symptomatically. A favorable response has been reported after the use of corticosteroids in some cases.⁽¹¹⁾ Some patients who survive acute or subacute MBD have subsequent dementia, but, partial or complete recovery is occasionally observed. Patients who survive must stop drinking alcohol, receive guidance and rehabilitation therapy, and undergo nutritional counseling.⁽⁴⁾

In the present case, the patient received large parenteral doses of thiamine and vitamin complexes but died due to infection with an extremely rare pathogen. *Rhodotorula mucilaginosa* is a Basidiomycetes fungus belonging to the family Sporidiobolaceae (filo Basidiomycota) and is present throughout the world.⁽¹³⁾ This organism can be found in aquatic and terrestrial environments and on the surfaces of mucous membranes of animals, including human beings.⁽¹⁴⁻¹⁶⁾ Although it was once considered a non-pathogenic microorganism, this agent is now recognized as potentially harmful, especially in the immunosuppressed.⁽¹⁷⁾ It has been directly associated

with infections of catheters and prosthetic grafts,^(16,18,19) endocarditis,^(19,20) peritonitis⁽²¹⁾ and meningitis.^(22,23) More recently, this microorganism has been implicated as a causative agent in onychomycosis.⁽²⁴⁾

A systematic review of 128 patients with proven infection by *Rhodotorula*⁽²⁵⁾ showed that the species *mucilaginosa* is the most commonly involved in human diseases, accounting for 74% of infections. Additionally, immunosuppressed patients and the elderly are more susceptible, particularly those subjected to invasive procedures (deep venous access, deployment of peritoneal dialysis catheters and surgical prostheses). The mortality rate is as high as 12%. This fungus is generally resistant to fluconazole, voriconazole and itraconazole; for this reason, the antimicrobial of choice is amphotericin B.^(25,26)

CONCLUSION

We hypothesize that this patient's malnutrition and chronic alcoholism caused some degree of immune system depression. Additionally, his protracted course in the intensive care environment made him particularly prone to this rare infectious agent.

RESUMO

A doença de Marchiafava-Bignami é uma entidade rara, caracterizada por uma degeneração primária do corpo caloso,

so, associada com o consumo crônico do etanol. A doença pode, ocasionalmente, ocorrer em pacientes não etilistas cronicamente desnutridos. Uma deficiência de vitaminas do complexo B é considerada como a hipótese etiopatogênica principal, uma vez que muitos pacientes obtiveram uma melhora após a administração desses compostos. Algumas vezes, entretanto, tal resposta terapêutica não foi observada. O diagnóstico definitivo da doença de Marchiafava-Bignami pode ser problemático e depende das características de estudos de neuroimagem, especialmente a ressonância magnética. Seu tratamento, dessa forma, é ainda controverso, com resultados variáveis. Como estão implicados fatores nutricionais, analogamente à encefalopatia de Wernicke, alguns autores recomendam a reposição de vitaminas do complexo B, particularmente da B1. O presente artigo relata a forma aguda da doença de Marchiafava-Bignami em um paciente masculino dependente do álcool, que apresentou discreta melhora após a administração parenteral das vitaminas do complexo B. Como consequência de suas más condições neurológicas e imunológicas, ele desenvolveu infecções pulmonares múltiplas e permaneceu, por longo tempo, na unidade de terapia intensiva. Seu óbito ocorreu por sepse causada por um fungo raro, o *Rhodotorula mucilaginosa*. O artigo é um relato clínico da evolução desse paciente, com a apresentação de seus dados de neuroimagem, acompanhada por uma revisão sobre doença de Marchiafava-Bignami e sobre as infecções por *Rhodotorula* dentro da perspectiva da unidade de cuidado intensivo.

Descritores: Encefalopatias; Doença de Marchiafava-Bignami/diagnóstico; Alcoolismo/complicações; Infecção; Imagem por ressonância magnética; Relatos de casos

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